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TITLE: Surgical Timing and Rehabilitation (STaR) for Multiple Ligament Knee Injuries (MLKIs): A Multicenter Integrated Clinical Trial

PRINCIPAL INVESTIGATOR: James Irrgang

CONTRACTING ORGANIZATION: University of Pittsburgh, Pittsburgh, PA 15219

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14. ABSTRACT – limit 200 words

The objective of this project is to conduct two parallel, multicenter randomized clinical trials to determine how the timing of surgery (early vs. delayed) and rehabilitation (early vs. delayed) affects time to return to military duty, work, and sports and knee-related patient-reported physical function for 690 military personnel and civilians between the ages of 16 and 55 with a multiple ligament knee injury. To date, we have received IRB approval for 14 sites and approval by HRPO for 5 sites. Additionally, 4 sites are currently under review by HRPO.

Research activities over the past year have included finalizing the detailed study protocol, approval of the DSMB to start recruitment, creation and testing of the central study database, bi-weekly training sessions for research coordinators, and monthly investigators calls. In the past 2 months, the coordinating center at Pitt has conducted site initiation visits at 5 sites in preparation for HRPO approval.

At this time, only the coordinating center at the University of Pittsburgh has been approved for recruitment and has recruited and randomized 3 participants since July 1, 2018. We anticipate recruitment will start at 4 sites in November 2018 and all sites will be actively recruiting by the end of February 2019.

15. SUBJECT TERMS

Multiple ligament knee injuries; knee dislocation; surgical timing; rehabilitation progression; return to pre-injury activity level, military duty, work and sports.

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
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INTRODUCTION:

While uncommon, multiple ligament knee injuries (MLKIs) present a considerable treatment challenge in service members, athletes, and the general population. Following a MLKI, individuals are frequently limited with higher demand activities such as in military training, physical labor and sports. Return to duty after combat-related MLKIs has been reported to be as low as 41% and substantially lower than return to work reported for civilians. There is controversy related to the optimal timing of surgery and post-operative rehabilitation for the treatment of MLKIs. Early surgical intervention may allow for repair of injured tissue but is associated with greater risk for joint stiffness and compartment syndrome, both of which will delay return to military, work and sports activity and participation. Delayed surgery has a lesser chance of stiffness but relies on use of grafts for reconstruction which may not provide the same stability as repair. Due to the extensive nature of the surgery for MLKI, expert opinion prefers delayed rehabilitation to protect the healing structures, but this has not been empirically tested. The best evidence for timing of rehabilitation is based on evidence following ACL reconstruction, where immediate range of motion and weight bearing is the current standard of care. Due to the lack of evidence for the timing of surgery and post-operative rehabilitation, a large-scale trial is needed to optimize the outcomes for these potentially devastating injuries. The overall objective of this project is to investigate the effects of timing of surgery (early vs. delayed) and timing of post-operative rehabilitation (early vs. delayed) for treatment of MLKIs in military personnel and civilians between the ages of 16 and 55. Aim 1: We will recruit and randomize 392 individuals with a MLKI to early vs. delayed surgery and early vs. delayed rehabilitation to determine the combined effects of timing of surgery and rehabilitation on the time to return to pre-injury military duty, work and sports. We hypothesize that early surgery, early rehabilitation and the combination of early surgery and early rehabilitation will lead to an earlier return to duty, work and sports and better patient-reported physical function. Aim 2: We will recruit and randomize 298 individuals with MLKI whose surgical timing cannot be randomized to early vs. delayed rehabilitation to determine the effects of timing of rehabilitation on the time to return to military duty, work and sports. We hypothesize that early rehabilitation will lead to an earlier return to duty, work and sports and better patient-reported physical function. The primary outcome will be time to return to pre-injury military duty, work and sports which will be assessed monthly from 6 to 24 months after randomization. Additionally, patient-reported physical function that will be collected 6, 12 and 24 months after randomization. Secondary outcomes will include additional knee-specific and generic patient-reported outcomes, recovery of range of motion, arthrofibrosis, residual laxity, complications/adverse events, re-injury and additional surgical procedures, which will be determined through usual-care clinical follow-up 1, 3, 6 and 9 to 12 months after surgery. Given the activity demands of military personnel, MLKIs represent a substantial cost and burden to the military health system. This project provides a unique opportunity to optimize surgical treatment and rehabilitation for individuals with a MLKI.

1. KEYWORDS:

Multiple ligament knee injuries; knee dislocation; surgical timing; rehabilitation progression; return to pre-injury activity level, military duty, work and sports.

2. ACCOMPLISHMENTS:

What were the major goals of the project?

The overall objective for this project is to investigate the effects of timing of surgery (early vs. delayed) and post-operative rehabilitation (early vs. delayed) for the treatment of military personnel and civilians that have a multiple ligament knee injury (MLKI). To achieve this objective, we will conduct two parallel randomized trials. The aims for these trials are:

Aim 1: To determine the effects of timing of surgery and post-operative rehabilitation on time to return to pre-injury level of military duty, work and sports and patient-reported physical function.

Aim 2: To determine the effects of timing of rehabilitation on time to return to pre-injury level of military duty, work and sports and patient-reported physical function.

The major tasks to complete these trials are:

Major Tasks	Start Date	End Date	Completion Status
Major Task 1: Study Start-Up	09/30/17	Ongoing	80%
Major Task 2: Subject Recruitment	07/02/18	Ongoing	<1%
Major Task 3: Clinical Monitoring & Quality Control Procedures	09/30/17	Ongoing	10%
Major Task 4: Subject Follow-Up	09/13/18	Ongoing	0%
Major Task 5: Study Governance	09/30/17	Ongoing	50%
Major Task 6: Analyze and Disseminate Results	-	-	0%

What was accomplished under these goals?

The description and status of each subtask are listed in the table below.

Tasks	Description of related subtask items	Start Date	End Date	Completion Status	Comments
Major Task 1: Study Start-Up					
1.Prepare Clinical Coordinating Center Regulatory Documents	1.a. Coordinating Center IRB Protocol Review & Approval	9/30/17	6/26/18	100%	Initial IRB protocol was approved on 12/7/17. IRB protocol was modified to reflect changes in the protocol based on discussion at the Initial Investigator Meeting. These changes did not affect the overall study aims

					and did not substantially alter the study risks. The modified protocol was approved on 6/26/18. The IRB received approval of continuing review on 10/12/2018.
	1.b. Coordinating Center HRPO Review & Approval	12/8/17	2/7/18	100%	
	1.c. Finalize Manual of Operations and Procedures (MOOP)	12/11/17		5%	The detailed clinical protocol was created and approved by the DSMB in 5/4/18 and shared with study investigators and research coordinators on 5/9/18. The MOOP is being drafted and will be finalized in Y2.
2.Prepare Local Site Regulatory Documents	2.a. Local Site IRB Protocol Review & Approval	12/11/17	Ongoing	58%	Fourteen sites have been submitted and approved by the University of Pittsburgh IRB (IRB of record).
	2.b. Local Site HRPO Review & Approval	8/3/18	Ongoing	20%	Nine sites have submitted documentation to the DoD for HRPO review. Five sites (see attachment B. Study Status Update) have received HRPO approval after modifications to the informed consent documents were made and approved by the IRB.
3.Execute Subcontract Agreements	3.a. Execute Subcontract & Data Use Agreements Between	9/30/17	Ongoing	95%	All subcontract agreements have been fully executed, except with St. Michael's Hospital.

	Coordinating Center and Sites				
4.Finalize Data Capture System	4.a. Finalize All Case Report Forms in REDCap	9/30/17	6/27/18	100%	
	4.b. Test Data Capture System	9/30/17	6/26/18	100%	The development and testing of the data capture system was completed on 6/26/18. The data capture system went 'live' on 6/27/18.
5.Final Randomization Schema	5.a. Finalize Randomization Schema – Specific Aim 1	9/30/17	5/18/18	100%	
	5.b. Finalize Randomization Schema – Specific Aim 2	9/30/17	5/18/18	100%	
6.Investigator Training	6.a. Investigator Meeting & Protocol Training	9/30/17	Ongoing	Ongoing	Initial protocol training occurred at the initial Investigators' Meeting that was held in Pittsburgh on 2/10/18. Additional training continued during the monthly Investigators' conference calls.
	6.b. Site Initiation Visit	6/5/18	Ongoing		The Site Initiation Visits (SIVs) began on 6/5/18. The SIVs are divided in 3 visits: 2 conducted remotely to discuss the study protocol and the rehabilitation training, and one in-person site visit to discuss the implementation of study. Aside from the University of Pittsburgh, 2 other sites have completed the site visits. Site visits for 6 sites have been scheduled and

					scheduling the other site visits is ongoing. (See attachment "B. Study Status Update"). We expect all site visits to be completed by Feb 2019.
Major Task 2: Subject Recruitment					
7.Distribution of Recruitment Materials		4/17/18	8/30/18		The University of Pittsburgh IRB approved recruitment materials were shared with study investigators and research coordinators on 8/30/18.
8.Subject Recruitment & Enrollment		7/2/18	Ongoing	< 1%	Recruitment started on 7/2/18 at the University of Pittsburgh. The first subject was enrolled in Trial 2 on 7/31/18.
9.Monthly Monitoring of Recruitment		7/2/18	Ongoing		Monthly conference calls with the Recruitment Committee are being held to discuss the recruitment for the study. Recruitment is also being reviewed and discussion on the monthly Executive Steering Committee and Investigators' calls.
Major Task 3: Clinical Monitoring & Quality Control Procedures					
10.Conduct Remote Interim Visit		Not started			No remote sites are active
11.Conduct Interim Site Visits		Not started			No remote sites are active.
12.Conduct Review of Monthly Quality Report		7/2/2018			The Coordinating Center is in the process of creating reports based on initial data collected at the University of Pittsburgh.
13.Prepare Materials for DSMB		2/26/18	Ongoing		The first DSMB

Materials				meeting was held on 4/17/18. The board approved the study protocol and template DSMB monitoring tables on 5/4/18. DSMB Meetings will be held every 6 months.
14.Monitor Data for AEs and SAEs	7/2/18	Ongoing		No adverse events occurred during the reporting period.
15.Monitor and Address Protocol Deviations	7/2/18	Ongoing		All protocol deviations are being recorded in REDCap data system. The study principal investigator and the research team discuss any and all protocol deviations at the weekly STaR Trial research meetings.
16.Monitor and Address Adherence and Fidelity to Randomization Assignment	7/2/18	Ongoing		Monitoring of the randomization assignment is taking place during the research team weekly meeting and the Executive Committee conference calls. One subject did not have the surgery performed within the timeframe to which the participant was randomized due to miscommunication between the research team and the clinical support staff. This protocol violation was recorded and reported to the IRB. The study team re-enforced with the clinical team that for the study participants, the date of surgery should only be

				discussed after the research coordinator randomizes the participant and provides the group assignment (early vs. delayed surgery) to the participant and clinical staff.
Major Task 4: Subject Follow-Up				
17.Collect Clinical Follow-Up Data	9/13/18	Ongoing	<1%	The clinical follow-up data collection for the first enrolled participant started with the 1-week post-operative visit (on 9/13/18).
18.Collect Physical Therapy Case Report Form	9/13/18	Ongoing	<1%	Adherence to the study rehabilitation protocol (determined by the surgeon and the physical therapist) was initiated at the 1-month post-operative visit for the first enrolled participant.
19.Conduct Subject Assessment of Rehabilitation Activity	9/13/18	Ongoing	<1%	Data on subjects' adherence to the rehabilitation guidelines was initiated with the 1-month post-operative clinical visit for the first enrolled participant.
20.Conduct Subject Assessment of Return to Activity	Not started		0%	This will start 6 months after the first participant was randomized.
21.Conduct Subject Assessment of Patient Reported Outcomes	Not started		0%	This will start after 6 months the first participant was randomized.
Major Task 5: Study Governance				
22.Monthly Conference Calls with Executive Steering Committee	9/30/17	Ongoing		Conference calls with the Executive Steering Committee were held twice a month during the first 3 quarters of study year 1. The

				conference calls are now held monthly to discuss study progress and recruitment.
23.Quartely Conference Calls for all Investigators to Discuss Study Progress	9/30/17	Ongoing	Partial	Conference calls with the study Investigators are held monthly to discuss study progress.
24.Quarterly Conference Calls for Study Governance Sub-Committees	9/30/17	Ongoing	Partial	Conference calls with the study committees were conducted prior to initiation of study recruitment. The Clinical Coordinating Center discusses study progress and recruitment monthly with the Recruitment Committee. The calls with the other committees are scheduled when deemed necessary.
25.Conference Calls for External Adverse Event Adjudication Committee Twice Per Year	Not started			Members of the External Adverse Event Adjudication Committee were identified, and they agreed to participate in the committee. We anticipate sending our first summary report on 1/15/19 to summarize the first six months of study conduct (from 7/1 to 12/31/18)
26.Annual Investigators Meeting	2/10/18	Ongoing		The first Annual Investigators Meeting was held in Pittsburgh on 2/10/18. Representative from 20 sites attended the meeting (either in person or via conference call). Our second meeting is

				planned in conjunction with the Extremity Warfare Injury Symposium for January 2019 in Washington, D.C.
Major Task 6: Analyze and Disseminate Results				
27.Final Data Cleaning &Verification	Not started			
28.Analysis of Data for Primary and Secondary Aims	Not started			
29.Preparation and Submission of Abstracts & Manuscripts for Primary and Secondary Aims	Not started			

What opportunities for training and professional development has the project provided?

Kathleen Poploski PT DPT has accepted the position of post-doctoral fellow to support the STaR Trial effective March 1, 2019. She will be responsible for overseeing and conduct the monthly remote research follow-up visits. Additionally, it is expected that she will enroll in a clinical research training certificate program at the University of Pittsburgh.

How were the results disseminated to communities of interest?

Nothing to report.

What do you plan to do during the next reporting period to accomplish the goals?

The plan for the next reporting period includes the following:

- Complete the subcontract agreement that is still pending (St. Michael's Hospital);
- Submit all required documentation for review and approval from the remaining sites to be onboarded onto the study by the University of Pittsburgh Institutional Review Board and to the DoD HRPO;
- Complete the on-boarding Site Initiation Visits (SIVs) to determine site personnel competence to implement the study protocol and procedures, and their readiness to begin recruitment for the study;
- Finalize and share Manual of Operating Procedures with all sites;
- Initiate and/or continue recruitment and randomization of subjects at all the study sites;
- Initiate and/or continue clinical and research follow-up visits to maximize subject retention and missing data:
- Continue with Clinical Monitoring Plan and meetings with the study committees.

3. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

Nothing to report.

What was the impact on other disciplines?

Nothing to report.

What was the impact on technology transfer?

Nothing to report.

What was the impact on society beyond science and technology?

Nothing to report.

4. CHANGES/PROBLEMS:

All of the protocol changes were deemed not to have been significant changes and were therefore not submitted to the Department of Defense for prior approval.

Changes in approach and reasons for change

Changes in the protocol that have been made since the beginning of project along with the rational for the change are summarized in the table below. These changes have been submitted for review and approval to the Data Safety and Monitoring Board on 5/4/2018 and by the University of Pittsburgh IRB on 6/26/2018.

Section	Original Proposal	Proposed Modification	Rationale for Modification
Exclusion criteria	Periarticular fracture (KD-V) that requires open reduction/internal fixation	Peri-articular and long bone (tibia/femur) fractures that preclude adherence to post-operative guidelines related to ROM and WB.	We do not want to exclude individuals who present with a periarticular or long bone (tibia/femur) fracture that would not affect post-operative ROM and WB guidelines.
Interventions: Rehabilitation	Early rehabilitation intervention would begin immediately	All participants will be NWB and in a brace locked in	There is a clinical concern for allowing WB and ROM in the

assignment	after surgery.	extension until disclosure of rehabilitation assignment to the participant at the first post-operative clinical visit.	immediate post-op phase. which could adversely affect healing of the incision. There are also logistic concerns in relaying the rehabilitation assignment to the participant who had recently been sedated/anesthetized.
Interventions: Early Rehabilitation	Unlimited motion and weight bearing as tolerated initiated within the 1st week after surgery.	Unlimited motion and weight bearing as tolerated initiated at the 1-week post-operative visit to orthopaedic surgeon.	There is a clinical concern for allowing WB and ROM in the immediate post-op phase, which could adversely affect healing of the incision. There are also logistic concerns in relaying the rehabilitation assignment to the participant who had recently been sedated/anesthetized.
Interventions: Rehabilitation	Early rehab: initiation of weight bearing and ROM exercises within the first post-op week after early surgical repair and/or reconstruction.	During the 1st week after surgery, all participants will wear a knee brace locked in extension and will be non-weight bearing. They will be instructed to perform isometric quadriceps exercises and self-patellar mobilizations.	Standardized exercises for all groups within 1st week post-operative due to concerns for over-stressing the tissues that were repaired or reconstructed.
Interventions: Delayed Rehabilitation	Delayed rehabilitation will be non-weight bearing and perform limited ROM (0-45°) for 4 weeks.	Delayed rehabilitation will include non-weight bearing with knee brace locked in extension with no	Proposed change is current standard of clinical care for patients with MLKI for the majority of study

		ROM for 4 weeks.	surgeons.
Interventions: Tissue Specific Considerations during Rehabilitation for Meniscus Repair (root or body repair)	Non-weight bearing flexion ROM will be limited to 90° for the early rehab, weight bearing flexion will be limited to no more than 30° and with no more than half body weight (i.e. bilateral weight bearing).	Brace locked in extension for 4 weeks for ambulation and weight bearing as tolerated (early rehab), avoid weight bearing motion in any range, non-weight bearing flexion ROM to 90° for 4 weeks (early rehab)	Proposed change is current practice for patients with MLKI and meniscus injury. For most meniscus root and body tears, weight bearing on a flexed knee could contribute to meniscal extrusion and could jeopardize healing of the repair.
Study Enrollment and Withdrawal: Participants Payment	Participants' payments will be processed by the University of Pittsburgh.	Participants' payments will be processed by each site.	Due to concerns for breach of confidentiality related to the need for an individual's social security number to process subject payment, each site will process participants' payment.
Study Enrollment and Withdrawal: Participants Payment	Participants will be paid $70 for informed consent and $35 for completion of baseline patient-reported outcomes.	Participants will be paid $50 for informed consent and $55 for completion of baseline patient-reported outcomes.	Redistribution of the baseline payments is based on the amount of time and participant burden associated with the informed consent process and completion of the baseline patient-reported measures. .
Study Schedule: Pre-screening in Emergency Department/Hospital and/or Orthopaedic Clinic.	Not listed in the original protocol.	Pre-screening (review of medical records by members of clinical care team) of patients that present with potential MLKI at Emergency Department, hospital and/or orthopaedic clinic.	Individuals with a MLKI could present to the emergency department, as a consult within the hospital or to the sport or trauma service orthopaedic clinics. The prescreening process will include review of the medical record for individuals with a MLKI

			by members of the clinical care team that would otherwise have access to the medical record information being reviewed to determine if individuals are potentially eligible for participation in the STaR Trial.
Study Schedule: Re-administer PROs for participants who undergo surgery greater than 4 weeks from baseline visit	Not listed in the original protocol.	Re-administer MLQoL, IKDC-SKF and PROMIS-PF within 1 week of surgery (pre-operative). This data will serve as the baseline outcome measures for participants enrolled in the trial that randomizes only to post-operative rehabilitation.	Participants' perspective of their functional status and quality of life may differ if surgical procedure is scheduled greater than 4 weeks from baseline visit.
Study Schedule: Baseline patient-reported measures for participants who present greater than 6 weeks from injury	All participants complete the MLQoL and IKDC-SKF at baseline.	Pending modification: Participants will complete the MLQoL – Activity Limitations Subscale at baseline, not completing the additional subscales of the MLQoL and IKDC-SKF.	Concern that individuals within 6 weeks of a major knee injury do not have sufficient exposure to the tasks and activities described on the MLQoL and IKDC-SKF to properly answer the items that are included on these outcome measures.
Study Procedures/ Evaluations: Other Patient-Reported Measures	Other PROs collected at baseline: - Tampa Scale for Kinesiophobia (17 items)	Other patient-reported measures collected at baseline: - Tampa Scale for Kinesiophobia (11	The Knee Self Efficacy and Internal Health Component of the Multidimensional Health Locus of Control Scales

	- Knee Self Efficacy Scale - Internal Health Component of the Multidimensional Health Locus of Control Scale - Brief Resilience Scale - Functional Comorbidity Index	items) - Brief Resilience Scale - Functional Comorbidity Index	were eliminated to reduce participant burden. The shortened version (11 items) of the Tampa Scale for Kinesiophobia was also selected to decrease the participant burden.

Actual or anticipated problems or delays and actions or plans to resolve them

We are behind on initial recruitment because we have experienced greater than anticipated delays to onboard all 24 remote sites as we worked with the remote sites, the University of Pittsburgh IRB and DoD HRPO to arrive at regulatory language that meets the requirements of all institutions. We have been working with the University of Pittsburgh IRB and DoD HRPO to ensure that documentation is submitted in a fashion that limits further delays. We have established excellent communication lines with both the IRB and HRPO and will work to maintain these lines of communication to facilitate on-boarding of sites. Figures 1 and 2 (below) illustrate the study recruitment projections, assuming all sites will be onboarded and recruiting by February 2019.

Because of the delays in on-boarding sites, we have not met our CY2018 goal to recruit 50% of the sample. Therefore, on our quad chart, we have updated the goals for CY2019 to reflect that we will recruit 75% of the sample and to finish recruitment in Q1 of CY2020. This will push final follow-up back to Q1 of 2022.

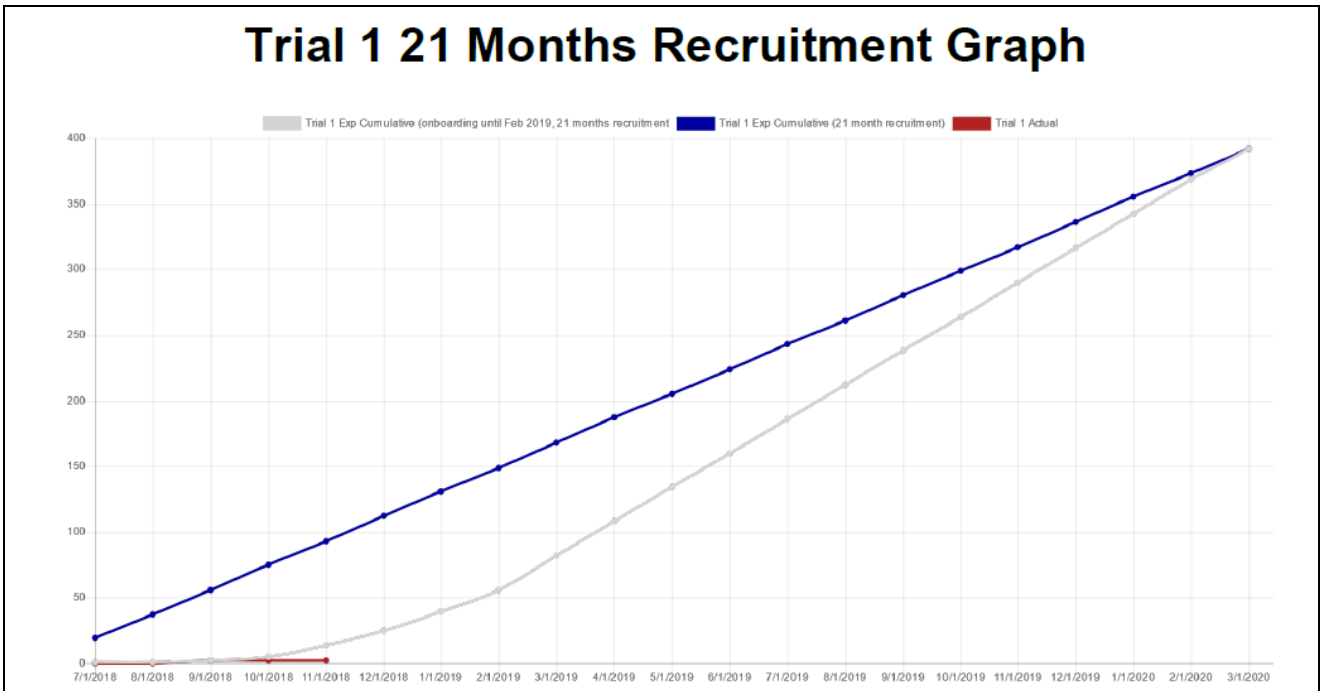


Figure 1. Actual vs. Expected Recruitment for Trial 1: Surgical Timing and Rehabilitation.

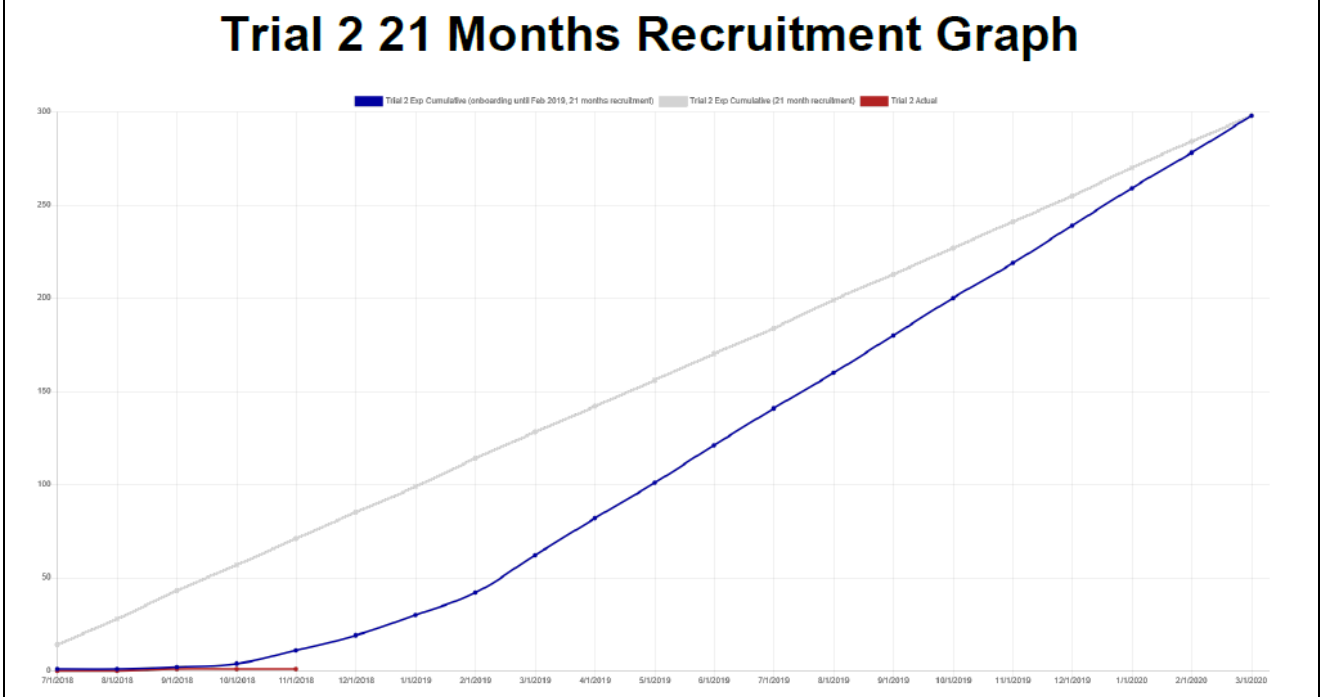


Figure 2. Actual vs. Expected Recruitment for Trial 2: Timing of Rehabilitation Only.

Changes that had a significant impact on expenditures

Because of the delays in on-boarding sites, our actual expenditures have been less than projected, but we expect that these funds will be expended as our enrollment and follow-up of subjects increases.

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Significant changes in use or care of human subjects

There have been no changes in the use or care of human subjects in this project. Initial IRB approval for the clinical coordinating center at the University of Pittsburgh was obtained on 12/7/2017 and the first continuing review of the project was obtained on 10/12/2018.

Date of Pitt IRB Approval	Site Onboarded
7/18/18	University of Virginia
8/8/18	TRIA/HealthPartners
	University of Cincinnati
	University of Kentucky
	University of Minnesota
	San Antonio Military Medical Center
8/29/18	Mayo Clinic
	University of Michigan
	University of New Mexico
	Washington University of St. Louis
	Brown University/Rhode Island Hospital
10/24/18	University of Connecticut
	University of Texas at Houston
	Wake Forest University
	Keller Army Community Hospital
	William Beaumont Army Medical Center

Significant changes in use or care of vertebrate animals

Not applicable.

Significant changes in use of biohazards and/or select agents

Not applicable.

5. PRODUCTS:

- **Publications, conference papers, and presentations**

Journal publications.

Nothing to report.

Books or other non-periodical, one-time publications.

Nothing to report.

Other publications, conference papers and presentations.

Irrgang JJ, Lynch AD, Burns TC, Harner CD , Levy BA, Owens BD, Schenck RC, Musahl V, Oostdyk AM, Popchak, AJ, Burnham JM, Patterson CM, Getgood A, Hodax J, Cooper JM, Ranawat AS, Marx RG, Coady CM, Wong IH, Macalena JA, Nelson BJ, Arciero RA, Edgar C, Cote M, Johnson DL, Jacobs C, Richter D, Treme G, Veitch AJ, Wascher DC, Black BS, Bailey L, Miller MD, Hart J. Mechanism, Presentation, Injury Pattern and Associated Injuries for Multiple Ligament Knee Injuries: A Multicenter Study from the Surgical Timing and Rehabilitation (STaR) Trial for MLKIs Network. American Academy of Orthopedic Surgeons Annual Meeting; New Orleans, LA; March 2018.

- **Website(s) or other Internet site(s)**

Nothing to report.

- **Technologies or techniques**

Nothing to report.

- **Inventions, patent applications, and/or licenses**

Nothing to report.

- **Other Products**

Nothing to report.

6. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Individuals from the Clinical Coordinating Center at the University of Pittsburgh

Name: **James J. Irrgang, PT PhD FAPTA**
Project Role: Principal Investigator

Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2.0 calendar months
Contribution to Project: Dr. Irrgang has been responsible for the overall design and conduct of the project and has served as the primary contact for all project-related correspondence. Dr. Irrgang has led the efforts of the study team at the University of Pittsburgh during the start-up phase of this multicenter clinical trial, including the efforts to obtain IRB approval, submission of the HRPO application, development of the study protocol and conducted the conference calls with the Executive Steering Committee, Investigators and Research Coordinators.

Name: **Volker Musahl, MD**
Project Role: Co-Principal Investigator/Qualified Surgical Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.0 calendar month
Contribution to Project: Dr. Musahl led all discussions and obtained consensus related to the surgical aspects of the study. This has included helping to refine and finalize the eligibility criteria as well as the surgical findings and procedures case report form. He has participated in the weekly STaR Trial Meetings as well as the Executive Steering Committee and Investigator conference calls. Dr. Musahl is also assisting with training investigators in the eligibility criteria for the study during the Remote Research Site Initiation Visits.

Name: **Andrew Lynch, PT, PhD**
Project Role: Co-Investigator/Qualified Rehabilitation Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2.0 calendar month
Contribution to Project: Dr. Lynch has planned and developed the procedures for the post-operative rehabilitation aspects of the study. He has also developed procedures to assess adherence to the rehabilitation program as randomized and contributed to the case report forms related to rehabilitation. He has participated in the weekly STaR Trial Meetings as well as the Executive Steering Committee and Investigator conference calls. He has led all discussions and obtained consensus related to the rehabilitation aspects of the study, and the rehabilitation training during the Remote Rehabilitation Site Initiation Visits.

Name: **Bryson Lesniak, MD**
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.0 calendar month
Contribution to Project: Dr. Lesniak is assisting with recruitment and retention of subjects in the study. He is also a member of the Recruitment Committee and has participated in the conference calls with the committee to review and discuss issues related with recruitment of subjects and in the Investigator conference calls. Dr. Lesniak is also assisting with investigators training in the eligibility criteria for the study during the Remote Research Site Initiation Visits.
Funding Support: Effort supported by University of Pittsburgh

Name: **Charity G. (Moore) Patterson, PhD**
Project Role: Biostatistician and Director of Data Coordinating Center
Researcher Identifier (e.g. ORCID ID): 0000-0002-0060-0124
Nearest person month worked: 1.0 calendar months

Contribution to Project: Dr. Patterson has designed the case report forms and build out of electronic data collection system, designed the adverse event adjudication process and designed and tested the randomization module. She is also planning and implementing the data coordinating center activities for trials. She has participated in the weekly STaR Trial Meetings as well as the Executive Steering Committee and Investigator conference calls.

Name: **Alexandra Gil, PT, PhD**
Project Role: Co-Investigator and Quality Control Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 1.0 calendar months
Contribution to Project: Dr. Gil has worked closely with Dr. Patterson to establish the data management procedures to ensure timely and accurate data collection. She has contributed to the development of case report forms, including the surgical and post-operative rehabilitation forms. She has also worked with Dr. Patterson and the Systems Analyst to ensure that the electronic data management system has the functionality to audit data quality and completeness.

Name: **M. Beatriz Catelani, PT, MS**
Project Role: Project Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 9 calendar months
Contribution to Project: Ms. Catelani has worked closely with Drs. Irrgang, Musahl & Lynch during all phases of project to ensure project is conducted in compliance with applicable research regulations. She has been responsible for planning the agenda, distributing meeting materials and maintaining meeting minutes for the Executive Steering Committee Conference calls. Additionally, she took the lead role in developing, editing and finalizing the detailed study protocol, and she is working on the Manual of Operating Procedures. She has assisted with the development of the plans for Clinical Monitoring, Adverse Event Reporting and Data and Safety Monitoring. She is also involved in planning, organizing and attending the Site Initiation Visits.

Name: **Megan Dalzell**
Project Role:Project Coordinator
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 9 calendar months
Contribution to Project: Ms. Dalzell has worked closely with Drs. Irrgang, Musahl & Lynch during all phases of project to ensure project is conducted in compliance with applicable research regulations. She has served as the key contact person for individuals at collaborating sites. She has assisted with the IRB and HRPO submission processes. She has planned the agendas and maintained minutes for the Investigators and Research Coordinators' conference calls. She is also involved in planning, organizing and attending the Site Initiation Visits.

Name: **Robert Winners**
Project Role: Systems Analyses (Electronic Data Capture Developer)
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2 calendar months

Contribution to Project: Mr. Winners built the electronic data collection system. In doing so, he has built and tested procedures for notifying teams of adverse events and problematic responses related to questions related to the emotional health of participants, procedures for administering patient-reported surveys, and an application for adverse event adjudication.

Name: **Gary Hlusko**
Project Role: Systems Analyses (Electronic Data Capture Developer)
Researcher Identifier (e.g. ORCID ID):
Nearest person month worked: 2 calendar months
Contribution to Project: Mr. Hlusko has built, formatted, tested and revised the case report forms so that they align with the study protocol.

Individuals from the Collaborating Clinical Research Sites

Institution	Name	Project Role	Contribution to Project	Whole Person Month	Funding Support
Keller Community Army Hospital	Matthew Posner	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Karen Peck	RC	Implement and conduct the study at the site	1 month	Institutional
San Antonio Military Medical Center	Travis Burns	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Germaine Herrera	RC	Implement and conduct the study at the site	1 month	Institutional
Tripler Army Medical Center	Craig Bottoni	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Jaime Chisholm	RC	Implement and conduct the study at the site	1 month	Institutional
Walter Reed National Military Medical Center	Jeffrey Giuliani	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	William Seymour	RC	Implement and conduct the study at the site	1 month	Institutional
William Beaumont Army Medical Center	Mark Pallis	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Raquel Resendez	RC	Implement and conduct the study at the site	1 month	Institutional
Rhode Island/Brown University	Brett Owens	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Kayleigh	RC	Implement and conduct	1	Institutional

	Sullivan		the study at the site	month	
TRIA/HealthPartners Institute for Education and Research	Bradley Nelson Jonathan Cooper	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Michael Obermeier Megan Reams	RC	Implement and conduct the study at the site	1 month	Institutional
Hospital for Special Surgery	Anil Ranawat	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Sava Turcan	RC	Implement and conduct the study at the site	1 month	Institutional
Mayo Clinic	Bruce Levy	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Jennifer Krogman	RC	Implement and conduct the study at the site	1 month	Institutional
University of Cincinnati	Brian Grawe	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Kim Hasselfed	RC	Implement and conduct the study at the site	1 month	Institutional
University of Connecticut	Robert Arciero	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Kelly Rushlow	RC	Implement and conduct the study at the site	1 month	Institutional
University of Kentucky	Darren Johnson	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Caitlin Conley	RC	Implement and conduct the study at the site	1 month	Institutional
University of Michigan	John Grant	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Jordyn Sessel	RC	Implement and conduct the study at the site	1 month	Institutional
University of Minnesota	Jeffrey Macalena	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Kristin Mathson	RC	Implement and conduct the study at the site	1 month	Institutional
University of New Mexico	Robert Schenck Jr	Site PI	Site oversight of the study and site	1 month	Institutional

			recruitment of subjects		
	Leorrie Atencio	RC	Implement and conduct the study at the site	1 month	Institutional
University of Texas Health Sciences Center at Houston	Christopher Harner	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Carmen Simon	RC	Implement and conduct the study at the site	1 month	Institutional
University of Virginia	Mark Miller	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Kaitlyn Shank	RC	Implement and conduct the study at the site	1 month	Institutional
University of Washington	Albert Gee	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Amy Cizik	RC	Implement and conduct the study at the site	1 month	Institutional
Washington University	Matthew Matava	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Wendy Holloway	RC	Implement and conduct the study at the site	1 month	Institutional
Wake Forest University	Brian Waterman	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Eboni Drummond	RC	Implement and conduct the study at the site	1 month	Institutional
Nova Scotia Health Authority	Catherine Coady	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Sara Sparavalo	RC	Implement and conduct the study at the site	1 month	Institutional
St. Michael's Hospital	Daniel Whelan	Site PI	Site oversight of the study and site recruitment of subjects	1 month	Institutional
	Ryan Khan	RC	Implement and conduct the study at the site	1 month	Institutional
University of Western Ontario d/b/a Lawson Health Research	Alan Getgood	Site PI	Oversight of the study and site recruitment of subjects	1 month	Institutional
	Stacey Wanlin	RC	Implement and conduct the study at the site	1 month	Institutional

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Nothing to report.

What other organizations were involved as partners?

The study collaborating institutions are listed in the table below. All of them have provided institutional support for planning and implementing the study at site.

Site 3: Keller Community Army Hospital 900 Washington Road West Point, NY 10996	**Site 4:** San Antonio Military Medical Center, 3551 Roger Brooke Drive, Fort Sam Houston, TX 78234	**Site 5:** Tripler Army Medical Center 1 Jarrett White Rd., Honolulu, HI 96859
Site 6: Walter Reed National Military Medical Center 8901 Wisconsin Avenue, Bethesda, MD 20889	**Site 7:** William Beaumont Army Medical Center 5005 N. Piedras St., El Paso, TX 79920	**Site 8:** Brown University 593 Eddy Street, Providence, RI 02903
Site 9: Health Partners Institute for Education and Research 8170 33rd Avenue South, P.O. Box 1524, Minneapolis, MN 55440	**Site 10**: Hospital for Special Surgery 535 East 70th Street, New York, NY 10021	**Site 11**: Mayo Clinic 200 First Street SW, Rochester, MN 55905
Site 12: TRIA Orthopaedic Center 8100 Northland Drive, Bloomington, MN 55431	**Site 13**: University of Cincinnati P.O. Box 670212 Cincinnati, OH 45267	**Site 14**: University of Connecticut Health Center 263 Farmington Avenue, Farmington, CT 06030
Site 15: University of Kentucky Research Foundation 800 Rose Street, Lexington, KY 40536	**Site 16:** University of Michigan, 3003 S. State St., Ann Arbor, MI 48109	**Site 17:** University of Minnesota 450 McNamara Alumni Center, 200 Oak Street SE, Minneapolis, MN 55455
Site 18: University of New Mexico Health Sciences Center 1 University of New Mexico, Albuquerque, NM 87131	**Site 19:** University of Texas Health Sciences Center at Houston 6400 Fannin St., Suite 1700, Houston, TX 77088	**Site 20**: University of Virginia 515 Ray C Hunt Drive, Charlottesville, VA 22903
Site 21: University of Washington 4333 Brooklyn Ave NE, Box 359472, Seattle, WA 98195	**Site 22**: Washington University Campus Box 1054, One Brookings Drive, St. Louis, MO 63130	**Site 23**: Nova Scotia Health Authority, Queen Elizabeth Health Sciences Center Halifax Infirmary Building, 4th floor, 1796 Summer Street, Halifax, Nova Scotia, Canada, B3H 3A6
Site 24: St. Michael's Hospital 30 Bond Street, Toronto,	**Site 25**: University of Western Ontario d/b/a Lawson Health	**Site 26:** Wake Forest University

Ontario, Canada, M5B 1W8	Research 750 Base Line Road, London, Ontario, Canada, N6C 2R5	Medical Center Boulevard, Winston-Salem, NC27157

SPECIAL REPORTING REQUIREMENTS

QUAD CHARTS:

Attached as Appendix A.

7. APPENDICES:

A. Quad Chart

B. Study Status Update

C. Recruitment Report

A. QUAD CHART

Surgical Timing and Rehabilitation (STaR) for Multiple Ligament Knee Injuries (MLKIs): A Multicenter Integrated Clinical Trial

Log Number - OR160109

PI's: Irrgang & Musahl **Org: University of Pittsburgh** **Award Amount: $4,476,920**

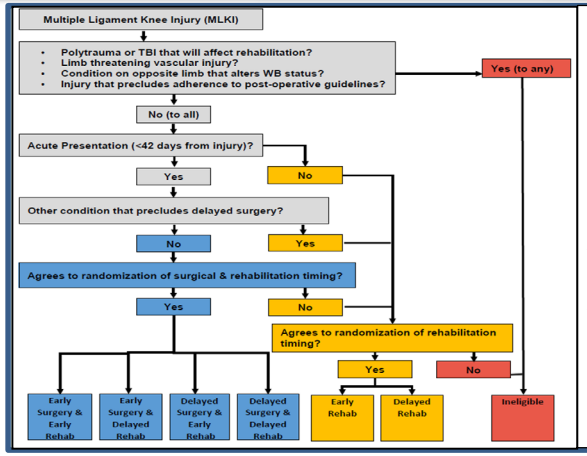
Study/Product Aim(s)

Aim 1: Determine the combined effects of timing of surgery & rehabilitation on time to return to duty, work & sports & patient-reported outcomes (PROs) for individuals with a MLKI.

Aim 2: Determine the effects of timing of rehabilitation on time to return to duty, work & sports and PROs for individuals with a MLKI.

Approach

Two parallel multicenter randomized clinical trials that enroll military personnel & civilians, between the ages of 16 & 55, with a grade 3 injury of 2 or more ligaments. Subjects will be randomized to early vs. delayed surgery and early vs. delayed rehabilitation for Aim 1 and early vs. delayed rehabilitation only for Aim 2. Subjects in both trials will be followed for 24 months to determine time to return to duty, work, and sports & PROs. Parallel trials will increase the generalizability of results to all-individuals presenting without life or limb threatening conditions to understand the impact of timing decisions on outcome for individuals with MLKI.



Study Flow Diagram. Individuals presenting with MLKI will be screened for inclusion & exclusion criteria. Individuals will be offered participation in a hierarchical fashion based on presentation. Blue boxes are associated with Aim 1 and yellow boxes with Aim 2.

Accomplishments: Obtained DSMB & HRPO approval; finalized detailed study protocol, initiated recruitment at coordinating site; bi-weekly Steering Committee and Research Coordinator & monthly Investigator Calls

Timeline and Cost

ACTIVITIES CY	17 q4	18	19	20	21 q1-3
Obtain IRB & HRPO Approvals					
Recruitment for Aims 1 & 2					
Follow-up for Aims 1 & 2					
Analyze & Disseminate Results					
Estimated Budget ($M)	$.34	$1.3	$1.0	$1.0	$.79

Updated: 30 September 2018

Goals/Milestones:

CY17 Goal – Study Start-Up
- ✓ Obtain IRB approval for coordinating center & local sites (partially)
- ✓ Obtain HRPO approval for coordinating center & local sites (partially)

CY18 Goals – Begin Recruitment & Follow-up
- ✓ Initiate recruitment
- ✓ Initiate follow-up

CY19 Goal – Complete Recruitment & Continue Follow-up
- ☐ Continue recruitment – target recruitment – 75% of total sample
- ☐ Continue interim follow-up

CY20 Goal – Complete Recruitment & Continue Follow-up
- ☐ Complete recruitment - 100%
- ☐ Continue interim & initiate final follow-up

CY21 Goal – Complete Follow-up & Analyze & Disseminate Results
- ☐ Complete all follow-ups
- ☐ Analyze data; write & submit abstracts & manuscripts

Budget Expenditure to Date

Projected Expenditure: $1,362,456

Actual Expenditure: $395,768.68 (through September 30, 2018)

B. STUDY STATUS UPDATE

#	SITE	PI	Coordinator (s)	Sub-Contract	IRB		DoD HRPO		Data Entry Training Complete	SIV				Site Recruitment Began
					Reliance Agreement	Pitt Approved	Submitted	Approved		Remote SIVs		On Site Complete	Action Items Complete	
										Research Complete	Rehab Complete			
01	University of Pittsburgh	James Irrgang Volker Musahl	Bea Catelani Megan Dalzell	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	7/2/2018
03	Keller Comm. Army	Matt Posner	Ken Cameron Karen Peck	✓	✓									
04	San Antonio Military	Travis Burns	Dennis Mann Germaine Herrera	✓	✓	✓	✓		✓					
05	Tripler Army	Craig Bottoni	Jaime Chisholm	✓	✓									
06	Walter Reed Army	John Dickens Jeffrey Giuliani	Timothy Mauntel William Seymour	✓	✓				✓					
07	William Beaumont Army	Mark Pallis	Raquel Resendez	✓	✓	✓			✓					
08	Brown/Rhode Island Hospital	Brett Owens	Kayleigh Sullivan	✓	✓	✓			✓					
09	TRIA (12)/HealthPartners Institute	Bradley Nelson Jonathan Cooper	Michael Obermeier Megan Reams	✓	✓	✓	✓	✓	✓	✓	✓	✓		
10	Hospital for Special Surgery	Anil Ranawat	Sava Turcan Caroline Boyle	✓	✓									
11	Mayo Clinic	Bruce Levy	Jennifer Krogman	✓	✓	✓	✓			Scheduled		✓		
13	University of Cincinnati	Brian Grawe	Kim Hasselfeld	✓	✓	✓			✓					
14	University of Connecticut	Robert Arciero	Kelly Rushlow	✓	✓	✓								
15	University of Kentucky	Darren Johnson	Cale Jacobs / Caitlyn Conley	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	
16	University of Michigan	John Grant	Jordyn Sessel	✓	✓	✓	✓	✓	✓	✓		Scheduled		
17	University of Minnesota	Jeff Macalena	Kristin Mathson	✓	✓	✓			✓	Scheduled		✓		
18	University of New Mexico	Robert Schenck	Sahar Freedman Christina Kurnik Leorrie Atencio	✓	✓	✓	✓	✓	✓	Scheduled		Scheduled		
19	University of Texas at Houston	Christopher Harner	Carmen Valerie Simon Lane Bailey	✓	✓				✓					
20	University of Virginia	Mark Miller	Kaitlyn Shank Stephan Bodkin	✓	✓	✓	✓	✓	✓	Scheduled				
21	University of Washington	Albert Gee	Kelsey Pullar	✓	✓									
22	Washington University of St. Louis	Matt Matava	Wendy Holloway Amanda Braun	✓	✓	✓	✓	Re-submitted 10/15/2018	✓	✓	Scheduled	Scheduled		
23	Nova Scotia Health Authority	Catherine Coady	Sara Sparavalo	✓	N/A									
24	St. Michaels Hospital	Daniel Whalen	Ryan Khan		N/A									
25	Western Ontario	Alan Getgood	Stacey Wanlin Ashley Martindale Andrew Firth	✓	N/A				✓	Scheduled		Scheduled		
26	Wake Forest University	Brian Waterman	Martha Holden Eboni Drummond Lisa McCorkle	✓	✓	✓	✓		✓					

C. RECRUITMENT REPORT

Recruitment Report 2018-10-08

STaR TRIAL

Surgical Timing and Rehabilitation For Multiligament Knee Injuries

University of Pittsburgh Physical Therapy Data Coordinating Center
100 Technology Drive
Pittsburgh, PA 15219
Date Generated: 2018-10-08

Data Lock: 10/05/2018

PreScreening by Site

Site	Start Date	Total PreScreened	Ineligible	Ineligible (%)
University of Pittsburgh	07/01/2018	15	7	46.67%
University of Cincinnati		0	0	N/A
HealthPartners Institute		0	0	N/A
Hospital for Special Surgery		0	0	N/A
Mayo Clinic		0	0	N/A
University of Michigan		0	0	N/A
University of Minnesota		0	0	N/A
University of New Mexico		0	0	N/A
Nova Scotia Health Authority		0	0	N/A
San Antonio Military		0	0	N/A
St Michaels Hospital		0	0	N/A
Tripler Army		0	0	N/A
TRIA Orthopaedics		0	0	N/A
University of Connecticut		0	0	N/A
University of Kentucky		0	0	N/A
University of Texas at Houston		0	0	N/A
University of Virginia		0	0	N/A
University of Washington		0	0	N/A
William Beaumont Army		0	0	N/A
Wake Forest University		0	0	N/A
Western Ontario University		0	0	N/A
Keller Army Community Hospital		0	0	N/A
Walter Reed Army		0	0	N/A
Washington University of St. Louis		0	0	N/A
Total		15	7	46.67%

This number reflects all charts & cases that were reviewed for potential participation in the study. Not all of these potential participants were approached

Reasons for Pre-Screen Criteria Failures (n = 7)

Reason	Answer	Met Criterion	Pre-Screen Failure (%)
Possibly has a multiple ligament knee grade III injury of 2 or more ligaments.	No	0	0.00%
Is at least 16 years of age and no more than 55 years of age	No	3	20.00%
Present for treatment 6 weeks or more from injury (Ineligible for Aim 1)(Potentially Eligible for Aim 2)	Yes	5	33.33%
Prior ligament surgery of involved knee	Yes	2	13.33%
Patellar or quadriceps tendon tear or avulsion	Yes	0	0.00%
Periarticular or long bone fracture that is anticipated to preclude adherence to post-operative guidelines	Yes	1	6.67%
Use of external fixator to maintain reduction of knee or soft tissue/open wound management for greater than 10 days.	Yes	1	6.67%
Inability to bear weight on contralateral leg	Yes	0	0.00%
Traumatic Brain Injury that limits ability to participate in post-operative care	Yes	0	0.00%
Vascular Injury that dictates timing of surgery (Ineligible for Aim 1)(Potentially Eligible for Aim 2)	Yes	1	6.67%
Vascular surgery that precludes early rehabilitation	Yes	0	0.00%
Multiple trauma that precludes performing surgery within 6 weeks of injury	Yes	0	0.00%
Multiple trauma that limits ability to participate in post-operative care	Yes	1	6.67%
Skin or soft tissue injury that dictates timing of surgery (Ineligible for Aim 1)(Potentially Eligible for Aim 2)	Yes	0	0.00%
Skin or soft tissue injury that precludes early weightbearing or range of motion	Yes	0	0.00%
Anticipated surgical procedure that precludes early weight bearing and range of motion	Yes	0	0.00%
Any condition that would preclude ability to comply with post-operative guidelines	Yes	0	0.00%

(Reasons why an individual was not approached for informed consent discussion)

In-Person Screening

Screenings by Site

Site	Screenings	Refused Consent	Consented	Eligible for Both Trials	Eligible for Both Trials (%)	Eligible for Rehab Only Trial	Eligible for Rehab Only (%)	Ineligible for both trials	Ineligible for both trials (%)
University of Pittsburgh	8	5	3	2	66.67%	1	33.33%	0	0.00%
Keller Army Community Hospital	0	0	0	0	N/A	0	N/A	0	N/A
San Antonio Military	0	0	0	0	N/A	0	N/A	0	N/A
Tripler Army	0	0	0	0	N/A	0	N/A	0	N/A
Walter Reed Army	0	0	0	0	N/A	0	N/A	0	N/A
William Beaumont Army	0	0	0	0	N/A	0	N/A	0	N/A
Brown University	0	0	0	0	N/A	0	N/A	0	N/A
HealthPartners Institute	0	0	0	0	N/A	0	N/A	0	N/A
Hospital for Special Surgery	0	0	0	0	N/A	0	N/A	0	N/A
Mayo Clinic	0	0	0	0	N/A	0	N/A	0	N/A
TRIA Orthopaedics	0	0	0	0	N/A	0	N/A	0	N/A
University of Connecticut	0	0	0	0	N/A	0	N/A	0	N/A
University of Kentucky	0	0	0	0	N/A	0	N/A	0	N/A
University of Michigan	0	0	0	0	N/A	0	N/A	0	N/A
University of Minnesota	0	0	0	0	N/A	0	N/A	0	N/A
University of New Mexico	0	0	0	0	N/A	0	N/A	0	N/A
University of Texas at Houston	0	0	0	0	N/A	0	N/A	0	N/A
University of Virginia	0	0	0	0	N/A	0	N/A	0	N/A
University of Washington	0	0	0	0	N/A	0	N/A	0	N/A
Washington University of St Louis	0	0	0	0	N/A	0	N/A	0	N/A
Nova Scotia Health Authority	0	0	0	0	N/A	0	N/A	0	N/A
St Michaels Hospital	0	0	0	0	N/A	0	N/A	0	N/A
Western Ontario University	0	0	0	0	N/A	0	N/A	0	N/A
University of Cincinnati	0	0	0	0	N/A	0	N/A	0	N/A
Wake Forest University	0	0	0	0	N/A	0	N/A	0	N/A
Total	8	5	3	0	0.00%	1	33.33%	0	0.00%

Number of individuals presenting to clinic for potential participation (i.e. passed all pre-screening criteria & presented to clinic)

Randomization By Site

Site	Eligible for Surgery Trial	Randomized Surgery Trial	Eligible for Surgery, Chose Rehab Only	Eligible for Rehab Only Trial	Total Eligible for Rehab Only	Pending Surgery for Rehab Only Trial	Randomized Rehab Only Trial
University of Pittsburgh	2	2	0	1	1	0	1
Keller Army Community Hospital	0	0	0	0	0	0	0
San Antonio Military	0	0	0	0	0	0	0
Tripler Army	0	0	0	0	0	0	0
Walter Reed Army	0	0	0	0	0	0	0
William Beaumont Army	0	0	0	0	0	0	0
Brown University	0	0	0	0	0	0	0
HealthPartners Institute	0	0	0	0	0	0	0
Hospital for Special Surgery	0	0	0	0	0	0	0
Mayo Clinic	0	0	0	0	0	0	0
TRIA Orthopaedics	0	0	0	0	0	0	0
University of Connecticut	0	0	0	0	0	0	0
University of Kentucky	0	0	0	0	0	0	0
University of Michigan	0	0	0	0	0	0	0
University of Minnesota	0	0	0	0	0	0	0
University of New Mexico	0	0	0	0	0	0	0
University of Texas at Houston	0	0	0	0	0	0	0
University of Virginia	0	0	0	0	0	0	0
University of Washington	0	0	0	0	0	0	0
Washington University of St Louis	0	0	0	0	0	0	0
Nova Scotia Health Authority	0	0	0	0	0	0	0
St Michaels Hospital	0	0	0	0	0	0	0
Western Ontario University	0	0	0	0	0	0	0
University of Cincinnati	0	0	0	0	0	0	0
Wake Forest University	0	0	0	0	0	0	0
Total	2	2	0	1	1	0	1

Reason for Exclusion for Participant Screened & Consented (n=1)

Reason	Answer	Number of Screened Failures	Screen Failures (%)
Had a multiple ligament grade III injury of 2 or more ligaments	No	0	0.00%
Is at least 16 years of age and no more than 55 years of age	No	0	0.00%
Prior ligament surgery of involved knee	Yes	0	0.00%
Patellar or quadriceps tendon tear or avulsion	Yes	0	0.00%
Periarticular or long bone fracture that is anticipated to preclude adherence to post-operative guidelines?	Yes	0	0.00%
Use of external fixator to maintain reduction of knee or soft tissue / open wound management for greater than 10 days	Yes	0	0.00%
Planned staged surgical treatment for multiligament knee injury	Yes	0	0.00%
Inability to bear weight on contralateral leg	Yes	0	0.00%
Traumatic Brain Injury that limits ability to participate in post-operative care	Yes	0	0.00%
Vascular Injury that dictates timing of surgery (Ineligible for Aim 1)(Potentially Eligible for Aim 2)	Yes	0	0.00%
Vascular surgery that precludes early rehabilitation	Yes	0	0.00%
Multiple trauma that precludes performing surgery within 6 weeks of injury	Yes	0	0.00%
Multiple trauma that limits ability to participate in post-operative care	Yes	0	0.00%
Skin or soft tissue injury that dictates timing of surgery (Ineligible for Aim 1)(Potentially Eligible for Aim 2)	Yes	0	0.00%
Skin or soft tissue injury that precludes early weightbearing or range of motion	Yes	0	0.00%
Anticipated surgical procedure that precludes early weight bearing and range of motion...	Yes	0	0.00%
Present for treatment 6 weeks or more from injury (Ineligible for Aim 1)(Potentially Eligible for Aim 2)	Yes	1	33.33%

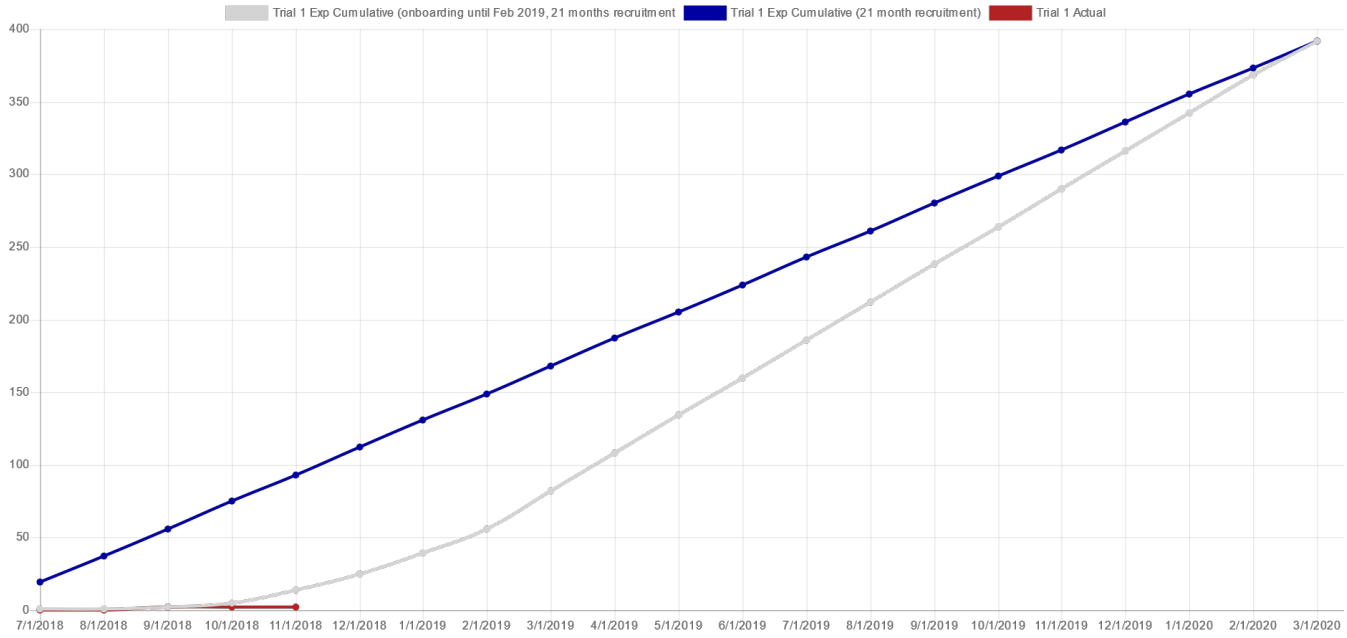
Rehabilitation Trial

Site	Eligible Before Surgery	Randomized Trial 2	Pending Surgery	Ineligible After Surgery
University of Pittsburgh	1	1	0	0
Keller Army Community Hospital	0	0	0	0
San Antonio Military	0	0	0	0
Tripler Army	0	0	0	0
Walter Reed Army	0	0	0	0
William Beaumont Army	0	0	0	0
Brown University	0	0	0	0
HealthPartners Institute	0	0	0	0
Hospital for Special Surgery	0	0	0	0
Mayo Clinic	0	0	0	0
TRIA Orthopaedics	0	0	0	0
University of Connecticut	0	0	0	0
University of Kentucky	0	0	0	0
University of Michigan	0	0	0	0
University of Minnesota	0	0	0	0
University of New Mexico	0	0	0	0
University of Texas at Houston	0	0	0	0
University of Virginia	0	0	0	0
University of Washington	0	0	0	0
Washington University of St Louis	0	0	0	0
Nova Scotia Health Authority	0	0	0	0
St Michaels Hospital	0	0	0	0
Western Ontario University	0	0	0	0
University of Cincinnati	0	0	0	0
Wake Forest University	0	0	0	0
Total	1	1	0	0

Ineligible after Surgery (Rehab Trial Only) (n=0)

Question	Answer	Total
Inability to bear weight on contralateral leg	Yes	0
Multiple trauma that limits ability to participate in post-operative care?	Yes	0
Patellar or quadriceps tendon tear or avulsion?	Yes	0
Periarticular or long bone fracture that precludes adherence to post-operative guidelines?	Yes	0
Skin or soft tissue injury that precludes early rehabilitation?	Yes	0
Surgical procedure that precludes early rehabilitation?	Yes	0
Traumatic Brain Injury that limits ability to participate in post-operative care?	Yes	0
Use of external fixator to maintain reduction of knee or soft tissue...	Yes	0
Vascular surgery that precludes early rehabilitation	Yes	0

Trial 1 21 Months Recruitment Graph



Trial 2 21 Months Recruitment Graph